

REMARKS

I. Claim Status

Reconsideration of the present application is respectfully requested. Claims 1-5, 7-13, 16, 19, 20, 22, 33 and 34 are pending. Claims 6, 14, 15, 17, 18, 21, and 23-32 are canceled without prejudice. Claim 1 has been amended to more clearly define the instant invention, and incorporates the subject matter of canceled claim 6. The amendments are supported by the specification and claims as originally filed, for example, at p. 8-9, ¶ 28; Example 1 at p. 36, ¶ 60; Example 2 at p. 36, ¶ 61 - p. 37, ¶ 62; and claim 6 as originally filed. No new matter has been added by way of this amendment.

II. Double Patenting

Claims 1, 2, 3, 5-10, 12, 13, 16, 19, 20, and 22 stand provisionally rejected for nonstatutory obviousness-type double patenting over claims 1, 3-11, and 17 of co-pending application serial no. 10/622,272. According to the Examiner, it would have been obvious to combine the optional ingredients noted in the '272 application to arrive at the presently claimed invention.

Since the rejection is provisional because the allegedly overlapping claims have not yet been patented, to the extent that claim scope overlaps in any patented case, Applicants will agree to submit a terminal disclaimer at such necessary time.

III. Rejections Under 35 U.S.C. § 112

Claims 4 and 11 stand rejected as unpatentable under 35 U.S.C. § 112, second paragraph, as being indefinite. According to the Examiner, it is unclear if Applicants intend to incorporate octoxyglycerin as an emollient solvent into independent claim 1 since dependent claim 11 is directed to ethyl hexyl glycerin, which the Examiner contends is octoxyglycerin. Thus, the Examiner alleges that it is not clear if Applicants claim octoxyglycerin twice in the instant composition.

Without conceding to the Examiner's contention, and to further the prosecution of the instant application, Applicants have canceled claim 11, and request that the rejection be withdrawn.

IV. Rejections Under 35 U.S.C. § 103(a)

- A. U.S. Patent No. 5,110,809 to Wang et al. in view of U.S. Patent No. 6,040,347 to Cupferman et al.

Claims 1, 4, 6-8, 11, 19, 20, 22, 33 and 34 stand rejected as unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,110,809 (to Wang et al.) in view of U.S. Patent No. 6,040,347 (to Cupferman et al.). The Examiner contends that Wang describes an antifungal gel formulation comprising imidazole antifungal agent, 17-ester, steroid, alcohol (*e.g.* ethanol), a gelling agent (*e.g.* hydroxypropyl cellulose or hydroxyethyl cellulose), water, emollient (*e.g.* PPG-20 methyl glucose ether), fragrance and preservative. The Examiner further alleges that Cupferman describes a gel for treating seborrhoeic skin comprising octoxyglycerol among other ingredients, and that it would have been obvious for an artisan of ordinary skill to combine Cupferman's octoxyglycerol with Wang's antifungal gel since the octoxyglycerol would have added further antimicrobial activity to the composition. The Examiner also states that even though Wang does not disclose the instantly claimed concentrations, it would have been obvious for the skilled artisan to adjust Wang's concentrations to arrive at the claimed ranges.

Applicants respectfully traverse the rejection and submit that the present claims are not obvious over the cited art. First, to support an assertion of obviousness, the Examiner must show that "all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." M.P.E.P § 2143. *See also KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (U.S. 2007), 82 USPQ2d at 1395.

Applicants submit that the claims have been amended to include the element "wherein the octoxyglycerin and antimicrobial agent are present in amounts which exhibit synergistic antimicrobial activity." Wang discloses an antifungal composition comprising an antifungal agent and a steroid, while Cupferman describes a composition for treating seborrhea comprising octoxyglycerol. Neither of the two references, considered separately or in combination, disclose a composition comprising two antimicrobial agents in amounts which exhibit a synergistic

antimicrobial activity. Thus, the cited references do not disclose all the elements of the amended claims, and do not render the claims obvious.

Second, evidence of unobvious or unexpected advantageous properties rebuts *prima facie* obviousness, and that the presence of a property not possessed by the prior art is sufficient evidence of nonobviousness. See M.P.E.P. 716.02(a); see also *In re Papesch*, 315 F.2d 381 (C.C.P.A. 1963). The claimed invention encompasses, *inter alia*, the unexpected discovery that octoxyglycerin, when combined with a second antimicrobial agent, exhibits a synergistic increase in the combined antimicrobial efficacy of the two antimicrobial agents. See the specification at pp. 8-9, ¶ 27.

As disclosed in Example 1 of the instant application (see pp. 34-36), compositions comprising either the antimicrobial octoxyglycerol (*i.e.* Sensiva SC50) or benzalkonium chloride ("BZK") alone were ineffective against *S. aureus*, but when present together in a single composition, the composition exhibited a surprisingly strong and unexpected effectiveness against *S. aureus*.

Tables 1 and 2 show that no significant antimicrobial activity against *S. aureus* was obtained with 2-5 percent [octoxyglycerol] . . . Similarly, 0.12 and 0.19 percent BZK exhibited minimal or no antimicrobial activity (Table 2). However, combinations of 1-2 percent Sensiva SC50 and 0.12-0.19 percent BZK showed 5000-33000 fold reduction in colony-forming units compared to control values (Table 2).

See the specification, Example 1, at p. 36, ¶60. Applicants submit that neither Wang nor Cupferman suggest or describe a composition comprising an antimicrobial agent which can exhibit synergistic antimicrobial effects when combined with a second antimicrobial agent, and Applicants discovery of such an unexpected result is indicative of the claims non-obviousness in view of the prior art.

Applicants also submit that a *prima facie* case of obviousness has not been established because it would not have been obvious to one skilled in the art to combine the octoxyglycerol antimicrobial of Cupferman with the antifungal composition of Wang. Wang is directed to a gel formulation of an antifungal which comprises an imidazole antifungal agent and a steroid antiinflammatory agent among other ingredients. See Wang at the abstract. As discussed in Applicants previous response, Wang explicitly states that:

Cream formulations often necessitate the use of emulsifiers or surfactants to maintain their physical stability and the use of antimicrobial preservatives to prevent microbiological contamination. These additives tend to generate an undesirable environment which can accelerate the hydrolysis of 17-ester steroids and the physical separation due to the salting out. . . . It was another object of the invention to provide topical gel formulations of mid-potency 17-ester steroids and imidazole antifungal agents which possess good dispersibility and good physical and chemical stability without refrigeration and without the need for special additives such as emulsifiers or surfactants or antimicrobial preservatives.

See Wang at col. 3, ll. 18-24; and col. 5, ll. 3-9 (emphasis added). Because Wang describes that its steroidal compound would be negatively impacted by the presence of a second antimicrobial agent, contrary to the Examiner's contention, a skilled artisan would seek to avoid introducing a second antimicrobial agent, such as octoxyglycerin, into the steroidal composition in order to maintain the compound's effectiveness.

Cupferman, which is directed to octoxyglycerol compositions for treating cutaneous disorders such as seborrhea (see Cupferman at the abstract), explicitly states that:

Use is commonly made, in combating . . . pathogenic agents, of active agents such as triclosan, hexamidine, hexetidine and benzalkonium chloride. However, the use of these active agents is not without side effects. . . . It is thus found that the need remains for topical active agents which have an effect on the pathologies related to microorganisms . . . while not exhibiting the disadvantages of the known compounds

See Cupferman at col. 1, ll. 28-31 and 40-45. Similar to the situation discussed above in Wang, a skilled artisan, in view of Cupferman, would avoid combining Cupferman's octoxyglycerol with a second antimicrobial agent, since the second agent would cause undesirable side effects which Cupferman seeks to avoid. Thus, in contrast to the Examiner's contention, a skilled artisan, in view of the cited references, would not be motivated to combine the antifungal composition disclosed by Wang with the octoxyglycerol of Cupferman; rather, the artisan would likely be motivated to keep the compounds separated.

Applicants submit that the collective teaching of the cited references does not render the claimed invention obvious because the cited art do not disclose all the limitations of the amended

claims, and the references provide a skilled artisan with no expectation of successfully practicing the claimed invention. Additionally, the non-obviousness of the claimed invention is further demonstrated by the surprising and unexpected results achieved by practicing the invention as claimed. Thus, Applicants respectfully request that the rejection be withdrawn.

B. U.S. Patent No. 4,478,853 to Chaussee in view of U.S. Patent No. 6,040,347 to Cupferman et al.

Claims 1-6, 13, 16, 19 and 20 stand rejected as unpatentable under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 4,478,853 (to Chaussee) in view of Cupferman. According to the Examiner, Chaussee teaches a composition containing ethanol, dimethicone, cyclomethicone, carbopol 940, glycerol, water, triethanolamine, and other components, including emulsifiers, and topical antiseptics such as benzalkonium chloride. As previously discussed, the Examiner also contends that Cupferman describes a gel for treating seborrhic skin comprising octoxyglycerol, among other ingredients. The Examiner alleges that it would have been obvious for an artisan of ordinary skill to combine Chaussee's composition with the octoxyglycerol of Cupferman to increase the antimicrobial activity of Chaussee's composition, rendering the claims obvious.

Applicants traverse the rejection. First, as previously discussed, the claims as amended require a synergistic antimicrobial effect between octoxyglycerin and a second antimicrobial agent. Neither of the cited references suggest or describe that a single composition comprising two antimicrobial agents (*i.e.* Cupferman's octoxyglycerol and Chaussee's benzalkonium chloride) would exhibit a synergistic antimicrobial effect. Thus, the collective teaching of the cited art does not disclose all of the claim elements, and do not render the claims obvious.

Second, as previously discussed, Cupferman discloses that commonly used antimicrobials, including benzalkonium chloride, produce undesirable side effects, and as such, a need exists for topical antimicrobials that are effective without causing such undesirable side effects. *See* Cupferman at col. 1, ll. 28-31 and 40-45. As such, Cupferman discloses that octoxyglycerol can be used as an antimicrobial in the absence of the side effect-inducing antimicrobial agents. Thus, in view of Cupferman, a skilled artisan would seek to avoid combining octoxyglycerol with other antimicrobials which would cause undesirable side effects. As noted by the Examiner, Chaussee's compound may include benzalkonium chloride as a

component of the composition. *See* Chaussee col. 8, l. 31. Because Cupferman discloses that such an agent is to be avoided in topical compositions, contrary to the Examiner's contention, a skilled artisan would not be motivated to combine Cupferman's octoxyglycerol with Chaussee's benzalkonium chloride.

Finally, as discussed above, the non-obviousness of the claimed invention is further supported by the surprising and unexpected results achieved by practicing the invention as claimed. In particular, Applicants surprisingly discovered that combining octoxyglycerol and a second antimicrobial agent in a single composition results in an unexpected antimicrobial synergy. *See* the specification, Example 1, at p. 36, ¶60. Thus, for the foregoing reasons, the claims are not obvious over the cited art, and Applicants respectfully request that the rejection be withdrawn.

C. U.S. Patent No. 4,478,853 to Chaussee in view of U.S. Patent No. 6,040,347 to Cupferman et al. and further in view of U.S. Patent No. 5,804,203 to Hahn et al.

Claim 9 stands rejected as unpatentable under 35 U.S.C. § 103(a) as obvious over Chaussee in view of Cupferman, and further in view of U.S. Patent No. 5,804,203 (to Hahn et al.). According to the Examiner, Cupferman describes a gel for treating seborrhic skin comprising octoxyglycerol, among other ingredients, while Chaussee teaches a composition containing ethanol, dimethicone, cyclomethicone, carbopal 940, glycerol, water, triethanolamine, and other components, including emulsifiers, and topical antiseptics such as benzalkonium chloride. The Examiner further contends that Hahn describes a topical formulation comprising the emulsifier Incroquat Behenyl TMS for reducing skin irritation, and that it would be obvious to combine such an emulsifier with the compositions of Cupferman and Chaussee, rendering the claims obvious.

Applicants respectfully traverse the rejection. The presently amended claims require a composition comprising antimicrobial synergistic amounts of octoxyglycerin and a second antimicrobial agent. As previously discussed neither Cupferman nor Chaussee, considered separately or in combination, disclose such a feature. Applicants further submit that Hahn, while disclosing topical anti-irritants comprising emulsifiers, is also silent with regard to antimicrobial agents that have synergistic antimicrobial effects when present in a single composition. Thus, combining Hahn's teaching with that of Cupferman and Chaussee fails to rescue the references

deficiencies, and can not be considered to render the claims obvious. For this reason, along with the previously discussed surprising and unexpected results achieved by practicing the claimed invention, the claims as amended are not obvious over the cited art, and Applicants respectfully request that the rejection be withdrawn.

D. U.S. Patent No. 4,478,853 to Chaussee in view of U.S. Patent No. 6,040,347 to Cupferman et al. and further in view of U.S. Patent No. 5,599,549 to Wivell et al.

Claim 10 stands rejected as unpatentable under 35 U.S.C. § 103(a) as obvious over Chaussee in view of Cupferman, and further in view of U.S. Patent No. 5,599,549 (to Wivell et al.). According to the Examiner, the combined disclosure of Cupferman and Chaussee describe all the elements of the rejected claim except for the silicone polymer dimethiconol fluid in dimethicone. The Examiner contends that Wivell discloses a personal cleansing and moisturizing composition comprising the claimed silicone polymer, and that it would be obvious for a skilled artisan to combine the silicone polymer of Wivell with the composition described by Cupferman and Chaussee, rendering the claims obvious.

Applicants respectfully traverse the rejection. As previously discussed, both Cupferman and Chaussee fail to describe all the elements of the claimed invention, specifically, the synergistic antimicrobial effect produced by combining octoxyglycerin and a second antimicrobial agent in a single composition. Wivell, like Cupferman and Chaussee, is silent with regard to any antimicrobial synergy that can be achieved by combining antimicrobial agents together. Thus, combining the teachings of the three references does not rescue their deficiencies, and does not describe all the elements of the claimed invention. For this reason, and further, because practicing the invention as claimed results in surprising and unexpected results, as previously discussed, Applicants assert that the claims as amended are not obvious in view of the cited art. Applicants respectfully request that the rejection be withdrawn.

V. Conclusion

In view of the above amendments and remarks, it is respectfully requested that the application be allowed and passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below. Applicants believe that no additional fees are due at this time. However, if any fees are required, the Commissioner is authorized to charge such fee to Deposit Account No. 02-4377.

Respectfully submitted,
BAKER BOTTS L.L.P.

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